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Tandem Zn-Brook Rearrangement/Ene-Allene Carbocyclization

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Dedicated to Professor Alain Krief

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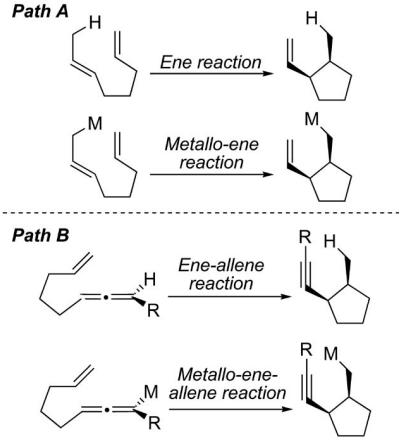
The addition of metalated alkynes to acylsilanes leads to the corresponding α-propargylsilanol derivatives. On addition of $ZnBr_2$, Zn-promoted Brook rearrangements take place to produce the propargyl/allenylzinc bromides, which undergo cyclization to give functionalized carbocycles as single diastereoisomers.

Introduction

The ene reaction, originally described by Alder,[1] is a powerful reaction in synthesis that has found many applications because of its highly organized transition state, which provides all the necessary characteristics for the control of relative and absolute configuration.[2] When both partners are simple alkenes and are linked together so as to provide for an intramolecular ene reaction, there is a preference for the formation of *cis*-disubstituted cyclopentane[3] and *trans*-disubstituted cyclohexane systems.[4] However, non-catalyzed ene reactions usually require elevated temperatures, and so the intramolecular metallo-ene reaction, in which a metal atom is transferred instead of a hydrogen atom (Scheme 1, path A), represents an interesting variant. Further synthetic manipulations of the resulting organometallic species can increase the molecular complexity. First described in 1970,[5] the metallo-ene reaction proceeds under milder conditions[6] and it has recently become abundantly clear that zinc-ene cyclizations are far superior to the more widely used magnesium-ene cyclizations.[7] Although the ene-allene reaction, by flash vacuum pyrolysis, was originally disclosed more than 25 years ago,[8] the metallo-ene-allene carbocyclization was developed more recently by our group (Scheme 1, path B).[9]



Scheme 1. Ene vs. metallo-ene reactions.

When 8-(trimethylsilyl)oct-1-en-7-yne (**1**) was metalated at the propargylic position with *s*BuLi, either in THF or Et_2O, no cyclization reaction of the resulting propargyl/allenyllithium species was observed even after the system had been allowed to stand at room temperature for several hours. The addition of 1 equiv. of magnesium salt to the lithium derivative did not lead to the cyclic product either. However, addition of 1 equiv. of $ZnBr_2$ to the lithium derivative at –20 °C resulted in a virtually quantitative cyclization reaction after stirring at room temperature. Hydrolysis of the reaction mixture led to the corresponding cyclopentane **3** in excellent isolated yields and as a single diastereoisomer (E = H, Scheme 2).

To explain the stereoselectivity of the reaction, a zinc-ene-allene transition state **2** in which the allenylzinc plays the role of the ene moiety and fixes the *cis* relationship of the two substituents was considered. When a substituent is present on the carbon skeleton, a unique isomer is still formed, and this was attributed to a preferred geometry in which the substituent preferentially occupies a pseudoequatorial position.

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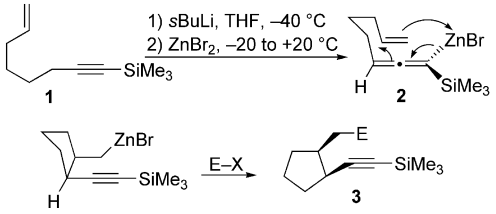
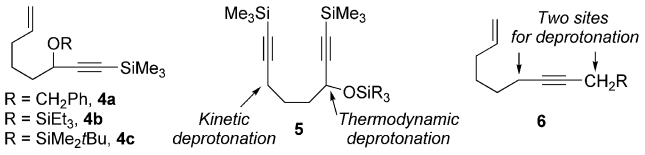


Scheme 2. Zn-ene-allene carbocyclization.

This strategy was extended to the stereoselective syntheses of polysubstituted tetrahydrofurans[10] and pyrrolidines[11] and to an efficient approach to angular and linear triquinane skeletons,[12] as well as to zinc-yne-allene[13] carbocyclization reactions. However, the direct metalation of propargylic benzyl ether **4a** (R = $CH_2C_6H_5$, Scheme 3) led instantaneously to a Wittig rearrangement,[14] whereas metalation of **4b** or **4c** (R = $SiEt_3$ or $SiMe_2tBu$, respectively) gave none of the cyclic product but instead a triene, presumably formed through translocation of the metal and an allylic proton.[15] Moreover, problems of regioselectivity may arise when two acidic sites are present in the molecule (i.e., kinetic vs. thermodynamic metalation reactions, for the metalation of **5**, Scheme 3)[13] or between two nearly equivalent acidic sites as in **6**. Therefore, although the Zn-ene-allene reaction is a very efficient and mild carbocyclization reaction, we recently wondered whether it might be possible to develop a simple synthetic solution that could overcome these limitations.



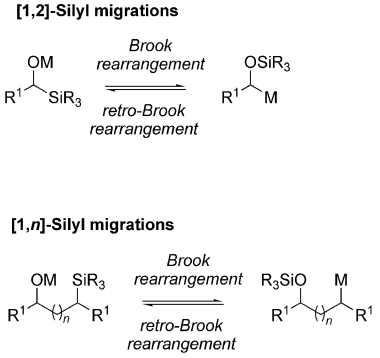
Scheme 3. Limitations of the method.

A possible solution to this problem would be to prepare propargyl/allenyl metal species such as **2** without any metalation step. How might we achieve such a transformation?

Results and Discussion

Fortunately, intramolecular 1,2-anionic migrations of silyl groups from carbon atoms to oxygen atoms were originally recognized and studied by A. G. Brook in the late 1950s and early 1960s (Scheme 4);[16] these rearrangements, extended to [1,*n*]-silyl migrations (such as the retro-Brook or West rearrangements),[17] have found increasing use in organic synthesis.[18,19]

The presence of an electron-withdrawing group (such as an alkynyl moiety in R^1 for the [1,2]-silyl migration) should stabilize the developing negative charge of the carbanion and then promote the migration of the silyl group from carbon to oxygen. However, in the case of the lithium salt **9a** of the α-silylpropargylic alcohol generated by the addition



Scheme 4. Brook vs. retro-Brook rearrangement.

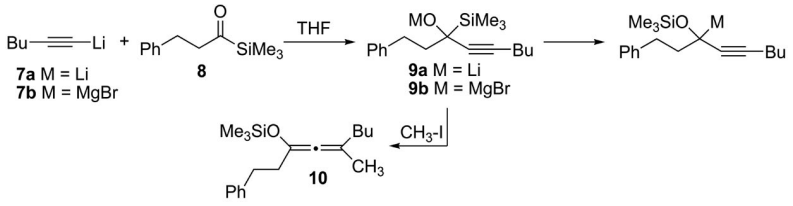
of the lithium acetylide **7a** to acylsilane **8**,[20] no Brook rearrangement was detected after hydrolysis. Because the stability of the alkoxide correlates with the ion pairing capability of the counterion, the highly aggregated state and tight ion pairing characteristics of lithium alkoxides stabilize intermediates such as **9a**.

Destabilization of alkoxides should therefore be achievable through the addition of reagents that chelate metal counterions, such as TMEDA. Even in the presence of TMEDA, NMP, or crown ether, however, no Brook rearrangement was observed. When the hexenylmagnesium species **7b** was used as nucleophilic species, only a 7% yield of the Brook product could be detected after hydrolysis.[21]

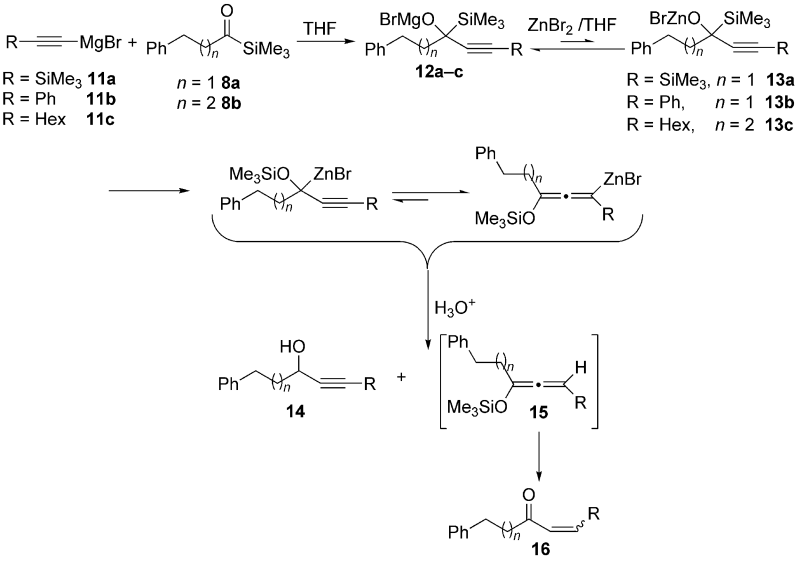
On the other hand, upon addition of methyl iodide to **9a**, the alkylated allenic Brook product **10** was formed in good yield. Hence, in the presence of a stoichiometric amount of base, the Brook rearrangement does not proceed and the equilibrium can only be switched towards the product by the presence of an electrophile (Scheme 5). Indeed, Brook rearrangements usually proceed when catalytic amounts of base are utilized and the typically rapid and essentially irreversible reaction takes place through protonation of the carbanion variously by the conjugate acid, by the starting alcohol, or by an excess of the starting alkyne possessing an acetylenic acidic hydrogen, but never when a stoichiometric amount of base is used.[22]

However, if one desires to have a specific carbanionic species in hand for subsequent reactions (i.e., carbometalation), the addition of an external electrophilic partner represents a limitation to the wide applicability of such processes. Can this equilibrium be displaced towards the formation of the propargyl/allenyl metal derivatives without addition of an electrophile? Considering that an additional factor for an efficient Brook rearrangement should be the stability of the formed organometallic species after migration, we hypothesized that a rearranged organozinc should afford extra stabilization through overlap of the nonbonding electrons of the oxygen atom and the filled d orbitals of the metal with the π-antibonding orbitals of the carbon–carbon bonds.[23]

When alkynylmagnesium bromides **11a**–**c** were added to acysilanes **8a** and **8b**, the α-silylmagnesium carbinols **12a**–**c** were formed in excellent yields (Scheme 6). After addition



Scheme 5. Effect on an electrophile on the Brook rearrangement.



Scheme 6. Zn-promoted Brook rearrangements.

of a solution of zinc bromide in THF, the corresponding zinc derivative **13a**–**c** underwent Brook rearrangements to afford two product types **14** and **16** after hydrolysis as shown in Scheme 6 and Table 1.

Table 1. Zinc-promoted Brook rearrangements.

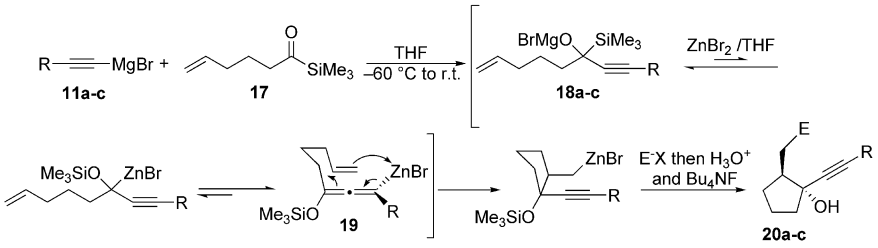
Entry	R	Starting material	**8** (*n*)	**14/16**[a]	Yield (%)[b]
1[c]	$SiMe_3$	**11a**	**8a** (1)	1.5:1	90
2[d]	Ph	**11b**	**8a** (1)	40:1	85
3[d]	Hex	**11c**	**8b** (1)	3:1	73

[a] Ratio determined on the crude product by NMR. [b] Determined after purification by column chromatography on silica gel. [c] Reaction mixture was stirred at room temperature overnight. [d] Reaction mixture was stirred at reflux overnight.

It is not surprising that compounds **13a**–**c** rearrange more readily than **12a**–**c** in view of the higher bond dissociation energy of the Mg–O bond (94 kcal mol^{-1}) relative to the Zn–O bond (68 kcal mol^{-1}).[24] Several zinc salts were tried for the conversion of **12a** to the Brook rearrangement products **14** and **16** [$ZnBr_2$ (90%), $ZnCl_2$ (65%), ZnI_2 (40%), $Zn(OTf)_2$ (32%)], and zinc bromide was found to be the most efficient for Brook rearrangements (zinc triflate was insoluble in THF). Moreover, THF was found to be the optimal solvent for the Brook rearrangements, because Et_2O and DME gave poorer results (15 and 40%, respectively).

With an efficient Zn-promoted Brook rearrangement to hand, we turned our attention to the combined Zn-Brook rearrangement/Zn-ene-allene cyclization reaction, starting with addition of compounds **11** to the ω-ene acylsilane **17**. Several representative alkynes such as **11a**–**c** were tested in this reaction, as described in Scheme 7 and Table 2. In all cases, acylsilane **17** was slowly added over a period of 30 min to afford the corresponding α-alkoxypropargylsilanes **18a**–**c**. Then, on addition of one equivalent of zinc bromide, the Brook rearrangements took place to give the corresponding propargyl/allenylzinc derivatives, which was immediately followed by diastereoselective Zn-ene-allene cyclization (Scheme 7).[25]

The reactions proceeded smoothly for all tested metalated alkynes [**11a** (R = $SiMe_3$), **11b** (R = Ph), **11c** (R = Hex), Entries 1 to 3, respectively in Table 2], although in the case of **11c** the cyclization could not be completed (the remaining being the hydrolyzed product obtained after the Brook rearrangement),[26] as judged from the formation of the carbocycles **20a**–**c** after hydrolysis. The formation of discrete organometallic species was checked by iodinolysis, as described for the formation of **20d** (Table 2, Entry 4). The *cis* configurations between methyl groups and alkynyl moieties were determined by comparison with literature data for **20a**[27] and assigned by analogy for all other compounds. This unique stereochemistry can be explained in terms of a zinc-ene-allene transition state **19** as illustrated in Scheme 7.



Scheme 7. Zn-Brook rearrangement/ene-allene cyclization.

Table 2. Tandem zinc-promoted Brook rearrangement/ene-allene carbocyclization.

Entry	R	Starting material	E–X	Products	*dr*[a]	Yield (%)[b]
1	$SiMe_3$	**11a**	H_3O^+	**20a**	>98:2	89
2	Ph	**11b**	H_3O^+	**20b**	>98:2	70
3	Hex	**11c**	H_3O^+	**20c**	>98:2	52
4	$SiMe_3$	**11a**	I_2	**20d**	>98:2	60

[a] Ratio determined on the crude product by NMR. [b] Determined after purification by column chromatography on silica gel.

Table 3. Tandem zinc-promoted Brook rearrangement/ene-allene carbocyclization of substituted acylsilanes **21** to afford cyclic products **24a**–**c**.

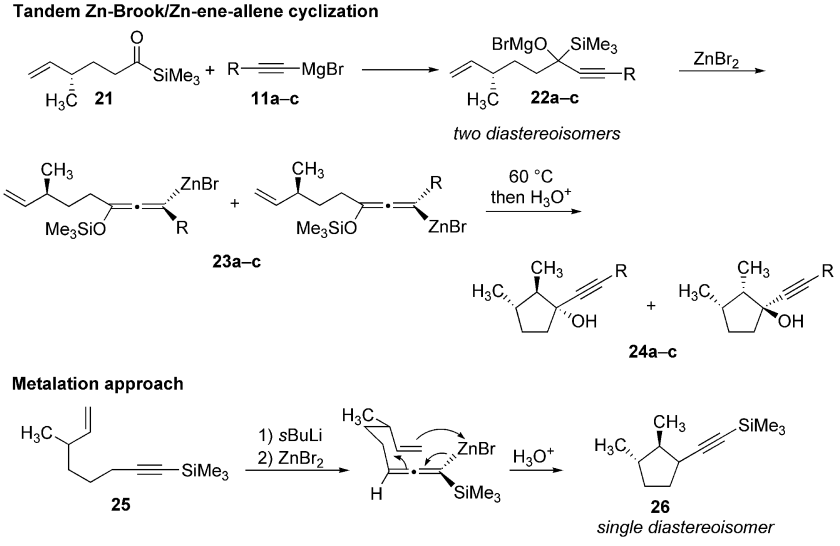
Entry	R	Starting material	Product	*dr*[a]	Yield (%)[b]
1	$SiMe_3$	**11a**	**24a**	1:1	73
2	Ph	**11b**	**24b**	1:1	67
3	Hex	**11c**	**24c**	1:1	62

[a] Ratio determined on the crude product by NMR. [b] Determined after purification by column chromatography on silica gel.

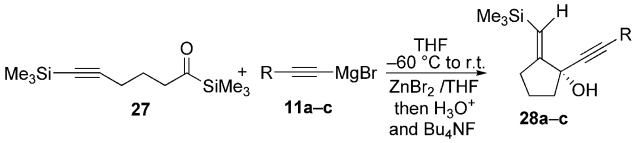
As would expected, when acylsilane **21**, possessing a substituent in the allylic position, was treated with alkynylmagnesium bromide derivatives **11a**–**c** the two diastereoisomers **22a**–**c** were obtained, in 1:1 ratios in all cases (Scheme 8 and Table 3). Further, when the zinc salt was added and the system was subjected to our tandem Zn-Brook rearrangement and Zn-ene-allene cyclization, pairs of cyclic isomers **24a**–**c** were obtained in good yields, also in 1:1 ratios.

It is interesting to note, however, that the cyclization of **25**, generated as described in our initial metalation approach, leads to a single diastereoisomer **26** after hydrolysis.[9] Therefore, we suggest that each diastereoisomer of the allenylzinc bromide **23** (with regard to the allylic stereogenic center), generated through our tandem reaction, leads to its own cyclic product **24**, because allenylzinc species are known to be configurationally stable,[28] and our ongoing research is intended to clarify this hypothesis.

Finally, we turned our attention to carbocyclization of alkynes to solve the problem of regioselectivity illustrated in Scheme 3 for the metalation of **5** when two acidic sites were present in the molecule (i.e., kinetic vs. thermodynamic metalation reactions). The acylsilane **27** was therefore first treated with alkynylmagnesium bromide derivatives **11a**–**c**, and the corresponding α-propargylsilanol species were then further treated with zinc bromide. After the transmetalation reactions, the Brook rearrangements followed by the Zn-yne-allene carbocyclizations gave, through *syn*-carbometalation reactions, the corresponding *exo*-alkylidene cyclopentyl species **28a**–**c** after hydrolysis (Scheme 9 and Table 4).



Scheme 8. Carbocyclization of allenylzinc species possessing allylic substituents.



Scheme 9. Tandem Zn-Brook rearrangement/ene-yne cyclization.

Table 4. Tandem zinc-promoted Brook rearrangement/yne-allene carbocyclization on substituted acylsilanes.

Entry	R	Starting material	Product	*E*/*Z*[a]	Yield (%)[b]
1	$SiMe_3$	**11a**	**28a**	>99:1	75
2	Ph	**11b**	**28b**	>99:1	63
3	Hex	**11c**	**28c**	>99:1	72

[a] Ratio determined on the crude product by NMR. [b] Determined after purification by column chromatography on silica gel.

Conclusions

In conclusion, the addition of metalated alkynes to acylsilanes leads to the initial formation of α-propargylsilanol salts. Addition of $ZnBr_2$ then promotes in situ Brook rearrangement followed by Zn-ene-allene (or Zn-yne-allene) cyclization to give the corresponding polysubstituted carbocycles in good isolated yields and as unique diastereoisomers with regard to the creation of quaternary and tertiary stereocenters. It is remarkable that these processes involve three successive rearrangements (Brook suprafacial, propargylic to allenylzinc and cyclization) and result in single diastereomers of the cyclization products.

Experimental Section

General: All reactions involving air- and moisture-sensitive compounds were carried out under argon, with flamed flasks and dry, oxygen-free solvents. Diethyl ether, tetrahydrofuran, and toluene were distilled under argon from sodium benzophenone ketyl. *n*BuLi and MeLi·LiBr were commercially obtained from Aldrich and titrated under argon with isobutanol in toluene (1 M), with 1,10-phenanthroline as indicator. All Grignard reagents were prepared and titrated under argon with isobutanol in toluene (1 M), with 2,2′-biquinoline as indicator. Unless otherwise noted, commercially available materials were used without further purification. Flash chromatography (FC) was performed with silica gel 60 (230–400 mesh). Thin layer chromatography was performed with precoated plates (silica gel 60, 0.25 mm). All NMR spectra were recorded at room temperature with Bruker Avance 300 and Bruker Avance 500 MHz instruments at operating frequencies of 300/500 MHz (^1H) or 75/125 MHz (^{13}C), respectively. Chemical shifts are referenced to the residual proton or carbon resonance of the deuteriated solvent (chloroform δ = 7.24 ppm for ^1H NMR or δ = 77.00 ppm for proton-decoupled ^{13}C NMR) with *J* in Hz. All the NMR spectroscopic data for our compounds were correlated with data from the literature (see references cited therein).

Acylsilanes were prepared according to literature procedures.[20,22,29]

Trimethyl(1-oxo-3-phenylpropyl)silane (8a): ^1H NMR ($CDCl_3$, 300 MHz): δ = 0.15 (s, 9 H), 2.77–2.82 (m, 2 H), 2.88–2.93 (m, 2 H), 7.12–7.21 (m, 3 H), 7.22–7.27 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = –4.8, 21.1, 35.0, 41.8, 128.0, 129.7, 133.8, 134.5, 246.1 ppm. FTIR (thin film): $\tilde{\nu}$ = 910, 997, 1081, 1162, 1253, 1350, 1411, 1443, 1642, 2856, 2925, 2955 cm^{-1}.

1-(Trimethylsilyl)hex-5-en-1-one (17): ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.16 (s, 9 H), 1.59 (quint, *J* = 7.5 Hz, 2 H), 1.99 (q, *J* = 7.0 Hz, 2 H), 2.57 (t, *J* = 7.2 Hz, 2 H), 4.91–4.98 (m, 2 H), 5.69–5.74 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = –3.2, 21.1, 33.2, 47.5, 115.0, 138.1, 248.3 ppm. FTIR (thin film): $\tilde{\nu}$ = 912, 997, 1079, 1091, 1162, 1249, 1351, 1411, 1443, 1642, 2856, 2927, 2956 cm^{-1}.

4-Methyl-1-(trimethylsilyl)hex-5-en-1-one (21): ^1H NMR ($CDCl_3$, 300 MHz): δ = 0.15 (s, 9 H), 0.94 (d, *J* = 6.6 Hz, 3 H), 1.43–1.54 (m, 2 H), 2.00–2.05 (m, 1 H), 2.54 (t, *J* = 7.4 Hz, 2 H), 4.86–4.93 (m, 2 H), 5.50–5.62 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –3.2, 20.3, 28.4, 37.5, 46.1, 113.2, 143.9, 248.3 ppm. FTIR (thin film): $\tilde{\nu}$ = 912, 995, 1077, 1090, 1162, 1249, 1353, 1411, 1443, 1639, 2856, 2927, 2956 cm^{-1}.

1,6-Bis(trimethylsilyl)hex-5-yn-1-one (27): ^1H NMR ($CDCl_3$, 300 MHz): δ = 0.03 (s, 9 H), 0.09 (s, 9 H), 1.60 (quint, *J* = 6.0 Hz, 2 H), 2.11 (t, *J* = 6.1 Hz, 2 H), 2.64 (t, *J* = 5.9 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –3.4, –3.3, 0.0, 19.0, 20.7, 46.4, 85.0, 106.4, 247.2 ppm. FTIR (thin film): $\tilde{\nu}$ = 911, 1044, 1248, 1351, 1407, 1430, 1645, 2173, 2900, 2957 cm^{-1}.

General Procedure for the Brook Rearrangements: EtMgBr in Et_2O (1 N, 1 equiv.) was added dropwise to a cold (0 °C) stirred solution of terminal alkyne in THF. The mixture was first allowed to warm to room temperature for 90 min and was then cooled to –78 °C for very slow introduction of the acylsilane **8** over a period of 30 min. After the addition was complete, the mixture was heated at reflux for 45 min, and a solution of $ZnBr_2$ in THF (1 N, 1 equiv.) was added at –60 °C. The reaction mixture was allowed to warm to room temperature over several hours and the evolution was followed by gas chromatography analyses of hydrolyzed aliquots. The reaction mixture was then quenched at –5 °C with aqueous HCl (1 M, 10 mL) and extracted with Et_2O (3 × 10 mL). The combined extracts were washed with saturated $NaHCO_3$ and stirred for at least 3 h with a few $Na_2S·9H_2O$ crystals that enabled the removal of all zinc salts before further purification. These were then removed by filtration, and the organic solution was washed with brine (2 × 15 mL), dried with $MgSO_4$, and concentrated to give the mixture of propargyl alcohols **14** (after removal of the silyl moiety) and α,β-unsaturated ketones **16**.

General Procedure for Desilylation: A solution of Bu_4NF (1 M, 1.05 equiv.) was added at room temperature to a solution of the corresponding silyl ether (1 mmol) in THF (3 mL). When the reaction was complete, the crude mixture was concentrated under reduced pressure. Brine was then added, and the aqueous phase was extracted five times with Et_2O. Next, the combined organic phases were washed once with brine, dried with $MgSO_4$, and purified by column chromatography (EtOAc/hexanes 5%) to give cyclic products as colorless liquids.

Compounds **14a** and **16a** were prepared by the general procedure with trimethyl(1-oxo-3-phenylpropyl)silane (130.2 mg, 0.5 mmol), (trimethylsilyl)acetylene (0.09 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol).

Compounds **14b** and **16b** were prepared by the general procedure with trimethyl(1-oxo-3-phenylpropyl)silane (130.2 mg, 0.5 mmol), phenylacetylene (0.07 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol).

Compounds **14c** and **16c** were prepared by the general procedure with trimethyl(1-oxo-3-phenylpropyl)silane (130.2 mg, 0.5 mmol), oct-1-yne (0.07 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol).

5-Phenyl-1-(trimethylsilyl)pent-1-yn-3-ol (14a): This compound was obtained after purification by column chromatography as a colorless liquid. 127.8 mg (55%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.12 (s, 9 H), 1.68 (s, 9 H), 1.92–2.00 (m, 2 H), 2.73 (t, J = 7.8 Hz, 2 H), 4.30 (t, J = 6.6 Hz, 1 H), 7.14–7.26 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –0.1, 31.4, 39.2, 62.2, 89.9, 106.4, 126.0, 128.4, 128.5, 141.3 ppm.

(*E*)-5-Phenyl-1-(trimethylsilyl)pent-1-en-3-one (16a): This compound was obtained after purification by column chromatography as a colorless liquid. 81.3 mg (35%). ^{1}H NMR (C_6D_6, 300 MHz): δ = 0.05 (s, 9 H), 2.52 (t, J = 7.7 Hz, 2 H), 2.90 (t, J = 7.6 Hz, 2 H), 6.42 (d, J = 19.5 Hz, 1 H), 6.88 (d, J = 19.2 Hz, 1 H), 7.02–7.10 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –1.9, 30.0, 41.0, 126.1, 128.4, 128.5, 141.2, 142.1, 147.0, 199.4 ppm. FTIR ($CHCl_3$): $\tilde{\nu}$ = 976, 1072, 1097, 1176, 1302, 1329, 1366, 1451, 1495, 1577, 1609, 1659, 1688, 3010, 3030 cm^{-1}. MS (GCMS): *m*/*z* calcd. for $C_{14}H_{20}OSi$ $[M]^{\cdot+}$ 232.4; found 232.0.

1,5-Diphenylpent-1-yn-3-ol (14b): This compound was obtained after purification by column chromatography as a yellow liquid. 4.8 mg (2%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.94–2.00 (m, 3 H), 2.73 (t, J = 8.1 Hz, 2 H), 4.30 (t, J = 6.6 Hz, 1 H), 7.12–7.25 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 31.4, 39.2, 62.2, 82.7, 89.9, 126.0, 126.0, 128.1, 128.3, 128.4, 128.8, 134.3, 141.1 ppm.

(*E*)-1,5-Diphenylpent-1-en-3-one (16b): This compound was obtained after purification by column chromatography as a yellow oil. 196.1 mg (83%). ^{1}H NMR (C_6D_6, 300 MHz): δ = 1.43 (dt, J_1 = 9.8, J_2 = 1.8 Hz, 2 H), 1.90 (t, J = 9.9 Hz, 2 H), 6.50 (dd, J_1 = 21.0, J_2 = 0.9 Hz, 1 H), 7.17–7.33 (m, 10 H), 7.61 (dd, J_1 = 20.9, J_2 = 1.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.0, 42.3, 126.0, 126.0, 128.1, 128.3, 128.4, 128.8, 130.4, 134.3, 141.1, 142.5, 199.1 ppm. FTIR ($CHCl_3$): $\tilde{\nu}$ = 976, 1072, 1097, 1176, 1302, 1329, 1366, 1451, 1495, 1577, 1609, 1659, 1688, 3010, 3030 cm^{-1}. HRMS (EI): *m*/*z* calcd. for $C_{17}H_{16}O$ $[M]^{\cdot+}$, 236.1201; found 236.1203.

1-Phenyldodec-4-yn-3-ol (14c): This compound was obtained after purification by column chromatography as a colorless liquid. 46.5 mg (18%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.86 (t, J = 6.9 Hz, 3 H), 1.24–1.27 (m, 4 H), 1.37–1.44 (m, 5 H), 1.46–1.64 (m, 2 H), 1.88 (quint, J = 6.9 Hz, 2 H), 2.20 (t, J = 6.9 Hz, 2 H), 2.64 (t, J = 7.7 Hz, 2 H), 4.20 (t, J = 6.3 Hz, 1 H), 7.13–7.29 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 18.9, 22.6, 25.7, 28.5, 29.0, 31.3, 36.2, 37.3, 64.6, 82.4, 88.2, 125.6, 128.2, 128.4, 142.5 ppm.

(*E*)-1-Phenyldodec-4-en-3-one (16c): This compound was obtained after purification by column chromatography as a colorless liquid. 142.1 mg (55%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.87 (t, J = 6.7 Hz, 3 H), 1.24–1.38 (m, 6 H), 1.41–1.45 (m, 2 H), 1.93 (quint, J = 7.5 Hz, 2 H), 2.17 (dq, J_1 = 7.2, J_1 = 1.2 Hz, 2 H), 2.53 (t, J = 7.4 Hz, 2 H), 2.63 (t, J = 7.2 Hz, 2 H), 6.06 (dt, J_1 = 15.9, J_2 = 1.2 Hz, 1 H), 6.72–6.82 (m, 1 H), 7.15–7.19 (m, 3 H),7.24–7.29 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 22.5, 25.7, 28.0, 28.8, 31.6, 32.4, 35.2, 39.2, 125.9, 128.3, 128.5, 130.2, 141.7, 147.5, 200.5 ppm. FTIR ($CHCl_3$): $\tilde{\nu}$ = 909, 977, 1100, 1229 1261, 1370, 1438, 1456, 1495, 1625, 1666, 1688, 2857, 2930, 2958, 3009 cm^{-1}. HRMS (EI): *m*/*z* calcd. for $C_{18}H_{26}O$ $[M]^{\cdot+}$ 258.1984; found 258.1984.

General Procedure for Brook Rearrangements Followed by Zinc-Ene-Allene Cyclization: A solution of EtMgBr in Et_2O (1 N, 1 equiv.) was added dropwise to a cold (0 °C) stirred solution of terminal alkyne in THF. The mixture was first allowed to warm to room temperature for 90 min and was then cooled to –78 °C for very slow introduction of the acylsilane over a period of 30 min. After the addition was complete, the mixture was heated at reflux for 45 min, and a solution of $ZnBr_2$ in THF (1 N, 1 equiv.) was added at –60 °C. The reaction mixture was either allowed to warm to room temperature in the case of **20a** or heated at 40 °C in the cases of **20b** and **20c** for a few hours (the evolution was followed by gas chromatography analyses of hydrolyzed aliquots). The reaction mixture was then quenched at –5 °C with aqueous HCl (1 M, 10 mL) and extracted with Et_2O (3 × 10 mL). The combined extracts were washed with saturated $NaHCO_3$, and stirred for at least 3 h with a few $Na_2S{\cdot}9H_2O$ crystals that enabled the removal of all zinc salts before further purification. These were then removed by filtration, and the organic solution was washed with brine (2 × 15 mL), dried with $MgSO_4$, and concentrated to give the unpurified cyclic product, which was further desilylated.

General Procedure for Desilylation: Bu_4NF (1 M, 1.05 equiv.) was added at room temperature to a solution of the corresponding silyl ether (1 mmol) in THF (3 mL). When the reaction was over the crude mixture was concentrated under reduced pressure. Brine was then added, and the aqueous phase was extracted five times with Et_2O. Next, the combined organic phases were washed once with brine, dried with $MgSO_4$, and purified by column chromatography (EtOAc/hexanes 5%) to give the cyclic products as colorless liquids.

***cis*-2-Methyl-1-[(trimethylsilyl)ethynyl]cyclopenanol (20a):** This compound was prepared by the general procedure with 1-(trimethylsilyl)hex-5-en-1-one (85 mg, 0.5 mmol), (trimethylsilyl)acetylene (0.09 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 87.3 mg (89%) of **20a** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.15 (s, 9 H), 1.11 (d, J = 6.6 Hz, 3 H), 1.30–1.32 (m, 1 H), 1.67–1.71 (m, 2 H), 1.87–2.00 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 0.0, 16.5, 20.6, 31.1, 40.8, 45.8, 78.7, 90.1, 107.3 ppm. HRMS ($C_{14}H_{28}OSi_2$, EI $M^{\cdot+}$ *m*/*z*); calcd. 263.2043; found 263.2038.

***trans*-2-Methyl-1-(phenylethynyl)cyclopentanol (20b):** This compound was prepared by the general procedure with 1-(trimethylsilyl)hex-5-en-1-one (85 mg, 0.5 mmol), phenylacetylene (0.07 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 70.1 mg (70%) of **20b** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.10 (d, J = 6.6 Hz, 3 H), 1.40–1.43 (m, 1 H), 1.56 (br s, 1 H), 1.73–1.78 (m, 2 H), 1.96–2.16 (m, 4 H), 7.27–7.43 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 16.5, 20.6, 31.2, 40.9, 46.1, 78.9, 85.9, 90.6, 122.9, 128.2, 128.2, 131.6 ppm. HRMS [$C_{14}H_{16}O$, EI $M^{\cdot+}$ (– H_2O) *m*/*z*]; calcd. 182.1096; found 182.1114.

***trans*-2-Methyl-1-(oct-1-ynyl)cyclopentanol (20c):**[25] This compound was prepared by the general procedure with 1-(trimethylsilyl)hex-5-en-1-one (85 mg, 0.5 mmol), oct-1-yne (0.07 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 54.2 mg (52%) of **20c** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.87 (t, J = 6.8 Hz, 3 H), 1.01 (d, J = 6.6 Hz, 3 H), 1.23–1.27 (m, 4 H), 1.31–1.39 (m, 2 H), 1.41–1.48 (m, 2 H), 1.51–1.57 (m, 2 H), 1.62–1.70 (m, 2 H), 1.82–1.97 (m, 3 H), 1.99–2.04 (m, 1 H), 2.20 (t, J = 6.9 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 16.3,

18.7, 20.4, 22.5, 28.4, 28.7, 30.9, 31.3, 40.9, 45.6, 68.1, 78.5, 86.4 ppm.

***trans*-2-(Iodomethyl)-1-[(trimethylsilyl)ethynyl]cyclopentanol (20d):**[25] This compound was prepared by the general procedure with 1-(trimethylsilyl)hex-5-en-1-one (85 mg, 0.5 mmol), (trimethylsilyl)-acetylene (0.09 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol), with addition of I_2 (6 equiv.) at –30 °C in THF (10 mL). The reaction mixture was allowed to warm to room temperature and stirred for an additional 2 h before the hydrolysis, and further treatment was then performed as usual to afford 96.7 mg (60%) of **20d** as a yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.15 (s, 9 H), 1.40–1.46 (m, 1 H), 1.67–1.72 (m, 2 H), 1.93–1.98 (m, 1 H), 2.11–2.15 (m, 2 H), 2.27 (s, 1 H), 2.30–2.35 (m, 1 H), 3.08 (t, J = 9.4 Hz, 1 H), 3.46 (dd, J_1 = 6.1, J_2 = 2.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –0.1, 7.2, 20.0, 31.4, 42.4, 53.2, 77.7, 91.8, 105.5 ppm.

2,3-Dimethyl-1-[(trimethylsilyl)ethynyl]cyclopentanol (24a): This compound was prepared by the general procedure with 3-methyl-1-(trimethylsilyl)hex-5-en-1-one (92.2 mg, 0.5 mmol), (trimethylsilyl)-acetylene (0.09 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 76.8 mg (73%) of **24a** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.15 (s, 9 H), 0.90–0.93 (m, 3 H), 0.97–1.03 (m, 3 H), 1.23–1.45 (m, 2 H), 1.58 (s, 1 H), 1.85–2.12 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –0.0, 11.3, 13.6, 16.0, 19.3, 29.8, 30.1, 34.2, 39.2, 40.0, 40.6, 49.4, 53.1, 78.8, 78.9, 89.8, 90.0, 107.8, 108.3 ppm.

2,3-Dimethyl-1-(phenylethynyl)cyclopentanol (24b): This compound was prepared by the general procedure with 3-methyl-1-(trimethylsilyl)hex-5-en-1-one (92.2 mg, 0.5 mmol), phenylacetylene (0.07 mL, 0.6 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 71.8 mg (67%) of **24b** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.95–1.03 (m, 3 H), 1.12 (d, J = 6.6 Hz, 3 H), 1.34–1.41 (m, 1 H), 1.52–1.64 (m, 1 H), 1.95–2.01 (m, 3 H), 2.15–2.30 (m, 1 H), 7.27–7.29 (m, 3 H), 7.39–7.42 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 11.5, 13.8, 16.2, 19.4, 29.9, 30.1, 34.3, 39.2, 40.1, 40.7, 49.6, 53.4, 79.0, 79.1, 85.8, 91.1, 91.7, 122.9, 128.1, 128.1, 128.2, 131.5, 131.6 ppm.

(*E*)-1-[2-(Trimethylsilyl)ethynyl]-2-[(trimethylsilyl)methylidene]cyclopentanol (28a):[25] This compound was prepared by the general procedure with 1,6-bis(trimethylsilyl)hex-5-yn-1-one (120 mg, 0.5 mmol), (trimethylsilyl)acetylene (0.09 mL, 0.06 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 99.9 mg (75%) of **28a** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.12 (s, 9 H), 0.16 (s, 9 H), 1.76–1.79 (m, 1 H), 1.82–1.97 (m, 3 H), 2.00–2.04 (m, 1 H), 2.31–2.43 (m, 1 H), 2.49–2.56 (m, 1 H), 5.93 (t, J = 2.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –0.7, –0.1, 22.0, 29.7, 41.2, 62.5, 89.2, 107.9, 121.6, 163.1 ppm.

(*E*)-2-[(Trimethylsilyl)methylidene]-1-(2-phenylethynyl)cyclopentanol (28b):[25] This compound was prepared by the general procedure with 1,6-bis(trimethylsilyl)hex-5-yn-1-one (120 mg, 0.5 mmol), phenylacetylene (0.07 mL, 0.06 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 85.2 mg (63%) of **28b** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.13 (s, 9 H), 1.84–1.95 (m, 4 H), 2.04–2.13 (m, 2 H), 2.46–2.49 (m, 1 H), 2.56–2.57 (m, 1 H), 6.02 (t, J = 2.4 Hz, 1 H), 7.28–7.30 (m, 3 H), 7.42–7.43 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –0.7, 22.0, 29.8, 41.4, 76.7, 84.7, 91.2, 121.6, 122.8, 128.2, 131.7, 163.3 ppm.

(*E*)-2-[(Trimethylsilyl)methylidene]-1-(oct-1-ynyl)cyclopentanol (28c):[25] This compound was prepared by the general procedure with 1,6-bis(trimethylsilyl)hex-5-yn-1-one (120 mg, 0.5 mmol), oct-1-yne (0.07 mL, 0.06 mmol), ethylmagnesium bromide (0.6 mL, 0.6 mmol), and $ZnBr_2$ (0.7 mL, 1 M solution in THF, 0.7 mmol). After purification by column chromatography, 91.4 mg (72%) of **28c** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.10 (s, 9 H), 0.87 (t, J = 3 Hz, 3 H), 1.23–1.30 (m, 5 H), 1.47–1.50 (m, 2 H), 1.51–1.56 (m, 2 H), 1.74–1.90 (m, 3 H), 1.97–1.99 (m, 1 H), 2.22 (t, J = 7.6 Hz, 2 H), 2.36–2.39 (m, 1 H), 2.49–2.50 (m, 1 H), 5.9 (t, J = 2.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = –0.7, 14.0, 18.7, 21.8, 22.5, 28.4, 28.6, 29.7, 31.3, 41.5, 82.3, 85.5, 120.6, 163.8 ppm.

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[1] K. Alder, F. Pascher, A. Schmitz, *Ber. Dtsch. Chem. Ges.* **1943**, *76*, 27.
[2] J. K. Whitesell in *Stereoselective Synthesis* (Eds.: G. Helmchen, R. Hoffmann, J. Mulzer, E. Schaumann), Houben-Weyl, Thieme Stuttgart, **1996**, E21, volume 5, p. 3271.
[3] For reviews, see: a) J. Dubac, A. Laporterie, *Chem. Rev.* **1987**, *87*, 319; b) K. Mikami, M. Shimizu, *Chem. Rev.* **1992**, *92*, 1021; c) B. B. Snider, *Acc. Chem. Res.* **1980**, *13*, 426.
[4] a) D. F. Taber in *Intramolecular Diels–Alder and Ene Reactions*, Springer, New York, **1984**; b) L. Tietze, U. Beifuss, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1042.
[5] a) H. Lehmkuhl, D. Reinehr, *J. Organomet. Chem.* **1970**, *25*, C47; b) H. Felkin, J. D. Umpleby, E. Hagaman, E. Wenkert, *Tetrahedron Lett.* **1972**, *13*, 2285; c) H. Felkin, L. D. Kwart, G. Swierczewski, J. D. Umpleby, *J. Chem. Soc., Chem. Commun.* **1975**, 242.
[6] a) W. Oppolzer, *J. Heterocyl. Chem.* **1982**, *6*, S41; b) W. Oppolzer, *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 38.
[7] a) W. Oppolzer, F. Schröder, *Tetrahedron Lett.* **1994**, *35*, 7939; b) N. Millot, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 7779; c) K. Deng, J. Chalker, A. Yang, T. Cohen, *Org. Lett.* **2005**, *7*, 3637; d) J. Chalker, A. Yang, K. Deng, T. Cohen, *Org. Lett.* **2007**, *9*, 3825.
[8] a) L. Skattebol, Y. Strenstrom, *Tetrahedron Lett.* **1983**, *24*, 3021; b) W. D. Hunstmann, Y. J. Li, P. Giannomore, *Isr. J. Chem.* **1985**, *26*, 88.
[9] C. Meyer, I. Marek, G. Courtemanche, J. F. Normant, *J. Org. Chem.* **1995**, *60*, 863.
[10] a) E. Lorthiois, I. Marek, C. Meyer, J. F. Normant, *Tetrahedron Lett.* **1995**, *36*, 1263; b) E. Lorthiois, I. Marek, J. F. Normant, *Bull. Chem. Soc. Fr.* **1997**, *134*, 5317.
[11] E. Lorthiois, I. Marek, J. F. Normant, *Tetrahedron Lett.* **1997**, *38*, 89.
[12] C. Meyer, I. Marek, J. F. Normant, *Tetrahedron Lett.* **1996**, *37*, 857.
[13] C. Meyer, I. Marek, J. F. Normant, N. Platzer, *Tetrahedron Lett.* **1994**, *35*, 5645.
[14] T. Nakai, K. Mikami, *Chem. Rev.* **1986**, *86*, 885.
[15] G. Courtemanche, J. F. Normant, *Tetrahedron Lett.* **1991**, *32*, 5317.
[16] a) A. G. Brook, *J. Am. Chem. Soc.* **1958**, *80*, 1886; b) A. G. Brook, C. M. Warner, M. E. McGriksin, *J. Am. Chem. Soc.*

1959, *81*, 981; c) A. G. Brook, N. V. Schwartz, *J. Am. Chem. Soc.* **1960**, *82*, 2435; d) A. G. Brook, B. Iachia, *J. Am. Chem. Soc.* **1961**, *83*, 827.

[17] R. West, R. Lowe, H. F. Stewart, A. Wright, *J. Am. Chem. Soc.* **1971**, *93*, 282.

[18] For recent reports on Brook rearrangements, see: a) T. E. Reynolds, M. S. Binkley, K. A. Scheidt, *Org. Lett.* **2008**, *10*, 5227; b) T. E. Reynolds, C. A. Stern, K. A. Scheidt, *Org. Lett.* **2007**, *9*, 2581; c) A. Tsubouchi, K. Onishi, T. Takeda, *J. Am. Chem. Soc.* **2006**, *128*, 14268; d) X. Linghu, J. R. Potnick, J. S. Johnson, *J. Am. Chem. Soc.* **2004**, *126*, 3070; e) D. A. Nicewicz, C. M. Yates, J. S. Johnson, *Angew. Chem. Int. Ed.* **2004**, *43*, 2652; f) X. Linghu, J. S. Johnson, *Angew. Chem. Int. Ed.* **2003**, *42*, 2534; g) X. Linghu, D. A. Nicewicz, J. S. Johnson, *Org. Lett.* **2002**, *4*, 2957; h) C. Bolm, A. Kasyan, P. Heider, S. Saladin, K. Drauz, K. Gunther, C. Wagner, *Org. Lett.* **2002**, *4*, 2265; i) T. E. Reynolds, A. R. Bharadwaj, K. A. Scheidt, *J. Am. Chem. Soc.* **2006**, *128*, 15382; j) D. A. Nicewicz, J. S. Johnson, *J. Am. Chem. Soc.* **2005**, *127*, 6170; k) W. Moser, *Tetrahedron* **2001**, *57*, 2065.

[19] For anion relay chemistry, see: a) A. B. Smith III, W.-S. Kim, W. M. Wuest, *Angew. Chem. Int. Ed.* **2008**, *47*, 7082; b) A. B. Smith III, D. S. Kim, *J. Org. Chem.* **2006**, *71*, 2547; c) A. B. Smith III, D. S. Kim, *Org. Lett.* **2005**, *7*, 3247; d) A. B. Smith III, D. S. Kim, *Org. Lett.* **2004**, *6*, 1493; e) A. B. Smith III, V. A. Doughty, Q. Lin, L. Zhuang, M. D. McBriar, A. M. Boldi, W. H. Moser, N. Murase, K. Nakayama, M. Sobukawa, *Angew. Chem. Int. Ed.* **2001**, *40*, 191; f) A. B. Smith III, Q. Lin, V. A. Doughty, L. Zhuang, M. D. McBriar, J. K. Kerns, C. S. Brook, N. Murase, K. Nakayama, *Angew. Chem. Int. Ed.* **2001**, *40*, 196.

[20] H. J. Reich, R. E. Olson, M. C. Clark, *J. Am. Chem. Soc.* **1980**, *102*, 1423.

[21] When phenylmagnesium bromide and (trimethylsilyl)ethynylmagnesium bromide were used as nucleophiles, 12 and 45% yields, respectively, of Brook products could be isolated.

[22] For representative examples, see: a) H. J. Reich, E. K. Eisenhart, R. E. Olson, M. J. Kelly, *J. Am. Chem. Soc.* **1986**, *108*, 7791; b) H. J. Reich, R. C. Holtan, C. Bolm, *J. Am. Chem. Soc.* **1990**, *112*, 5609; c) H. J. Reich, M. J. Kelly, *J. Am. Chem. Soc.* **1982**, *104*, 1119; d) H. J. Reich, M. J. Kelly, R. E. Olson, R. C. Holtan, *Tetrahedron* **1983**, *39*, 949.

[23] For representative examples from our group in which organozinc promotes some unusual reactivity behavior, see: a) I. Marek, *Chem. Eur. J.* **2008**, *14*, 4300; b) T. Cohen, H. Gibney, R. Ivanov, E. A. H. Yeh, I. Marek, D. P. Curran, *J. Am. Chem. Soc.* **2007**, *129*, 15405; c) G. Kolodney, G. Sklute, S. Perrone, P. Knochel, I. Marek, *Angew. Chem. Int. Ed.* **2007**, *46*, 9291; d) I. Marek, G. Sklute, *Chem. Commun.* **2007**, 1683; e) G. Sklute, I. Marek, *J. Am. Chem. Soc.* **2006**, *128*, 4642; f) G. Sklute, D. Amsallem, A. Shibli, J. P. Varghese, I. Marek, *J. Am. Chem. Soc.* **2003**, *125*, 11776; g) S. Farhat, I. Zouev, I. Marek, *Tetrahedron* **2004**, *60*, 1329; h) A. Abramovitch, J. P. Varghese, I. Marek, *Org. Lett.* **2004**, *6*, 621; i) I. Marek, *Tetrahedron* **2001**, *58*, 9463; j) I. Creton, I. Marek, J. F. Normant, *Synthesis* **1996**, 1499; k) I. Marek, D. Beruben, J. F. Normant, *Tetrahedron Lett.* **1995**, *36*, 3695; l) I. Creton, H. Rezaei, I. Marek, J. F. Normant, *Tetrahedron Lett.* **1999**, *40*, 1899.

[24] *Lange's Handbook of Chemistry*, 15th ed. (online version) (Ed.: J. A. Dean), McGraw–Hill, New York, **1999**.

[25] R. Unger, T. Cohen, I. Marek, *Org. Lett.* **2005**, *7*, 5313.

[26] The Zn-ene-allene carbocyclization is faster for **11a** and **11b** than for **11c**.

[27] a) J. Battioni, M. L. Capmau, W. Chodkiewicz, *Bull. Chem. Chim. Fr.* **1969**, *3*, 976; b) P. Cannone, M. Bernatchez, *J. Org. Chem.* **1986**, *51*, 2147.

[28] a) J.-F. Poisson, F. Chemla, J. F. Normant, *Synlett* **2001**, 305; b) J.-F. Poisson, J. F. Normant, *J. Am. Chem. Soc.* **2001**, *123*, 4639; c) J. A. Marshall, N. D. Adams, *J. Org. Chem.* **1998**, *63*, 3812; d) J. A. Marshall, N. D. Adams, *J. Org. Chem.* **1999**, *64*, 5201; e) J. A. Marshall, G. M. Schaaf, *J. Org. Chem.* **2001**, *66*, 7825.

[29] a) C. Hammaecher, I. Ouzzane, C. Portella, J. P. Bouillon, *Tetrahedron* **2005**, *61*, 657; b) P. Janlowski, K. Plesniak, J. Wicha, *Org. Lett.* **2003**, *5*, 2789.

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